Information Disclosure Statement

A copy of the 1449 form submitted with the Information Disclosure Statement (IDS) filed on July 5, 2001, is being submitted herewith, along with a copy of the date-stamped postcard receipt. The IDS was timely filed under 37 C.F.R. §1.97(b). Therefore, no fee is necessary. Entry of the IDS is respectfully requested.

Priority

The Examiner states that amendment of the specification is required because no restriction of claims ever occurred in the '119 application and the instant specification is not a duplicate of the '119 specification. Neither 37 C.F.R. §1.53(b) nor 35 U.S.C. §§120 or 121 require that the parent of a divisional application have been subject to a restriction requirement. Nevertheless, to obviate the rejection, the related applications paragraph has been amended to state that the present application is a continuation of U.S. Patent Application Serial No. 09/133,119 and to include the patent number for the issued '119 application. The instant specification is identical to the '119 specification except that the instant specification has been revised to incorporate amendments filed in the parent application and to correct minor typographical errors and informalities.

If the Examiner desires, Applicants will produce a redlined version or other comparison document comparing this application with the immediate parent thereof. No new matter has been added.

Rejection of Claim 3 Under 35 U.S.C. §102(b)

Claim 3 is rejected under 35 U.S.C. §102(b) as being anticipated by either of Hardmann *et al.* or Jarvis *et al.* The Examiner states that Hardmann discloses an isolated nucleic acid of a light chain murine variable region which would hybridize under conditions of moderate stringency to the complement of SEQ ID NO: 2. The Examiner further states that Jarvis discloses an isolated nucleic acid of a heavy chain murine variable region which would hybridize under conditions of moderate stringency to the complement of SEQ ID NO: 4.

Claim 3 has been cancelled, thus rendering the rejection moot. Reconsideration and withdrawal of the rejection are respectfully requested.

Rejection of Claims 1-23 Under 35 U.S.C. §103(a)

Applicants acknowledge the obligation under 37 C.F.R. §1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention is made. The subject matter of the claims was commonly owned at the time of the invention.

Claims 1-23 are rejected by the Examiner under 35 U.S.C. §103(a) as being unpatentable over any of Rathjen *et al.* or Yone *et al.* or Moeller *et al.* or Hirai *et al.* or Fendly *et al.* or Meager *et al.* or Liang *et al.* or Bringman *et al.* or Exley *et al.* or Yan *et al.*, all in view of Cabilly *et al.* The Examiner states that any of Rathjen *et al.* or Yone *et al.* or Moeller *et al.* or Hirai *et al.* or Fendly *et al.* or Meager *et al.* or Liang *et al.* or Bringman *et al.* or Exley *et al.* or Yan *et al.* teach neutralizing antibodies to human TNF-α, and Cabilly *et al.* teach the isolation of mRNA encoding recombinant antibodies and the transfer of the polynucleotide into an expression vector. Therefore, according to the Examiner, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to isolate the polynucleotides encoding the prior art antibodies and clone them into expression vectors.

Applicants respectfully traverse this rejection. Rathjen *et al.*, Yone et al.; Moeller *et al.*; Liang, *et al.*; Meager, *et al.*; Fendly *et al.*; Bringman, *et al.*; Hirai, *et al.*; Exley *et al.* and Yan *et al.* described rodent or murine mAbs specific for recombinant human TNF. However, none of the primary references cited by the Examiner characterize isolated nucleic acid molecules for the described antibodies, much less disclose the sequences recited in Applicants' claims. Cabilly *et al.* do not teach or suggest TNF neutralizing antibodies. Rather, Cabilly *et al.* merely describe the general method of isolating mRNA encoding recombinant antibodies and transferring the polynucleotides into an expression vector.

The pending claims are rejected based on prior art teachings of antibodies (proteins) that bind to TNF-α. The Examiner states that based on the teachings of Cabilly *et al.*, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to isolate the polynucleotides encoding the prior art antibodies and clone it into expression vectors.

However, this is the proposition the United States Court of Appeals for the Federal Circuit rejected in the case of *In re Bell*, 991 F.2d 781; 26 U.S.P.Q.2d 1529 (Fed. Cir. 1993) (attached hereto as Exhibit). The claims at issue were directed to nucleic acid molecules

containing human sequences which code for human insulin-like growth factors I and II (IGF), and sequences complementary to same and fragments of same which selectively hybridize to hIGF DNA. The relevant prior art consisted of two publications. One reference disclosed the amino acid sequences for IGF-I and IGF-II and the other described a general method for isolating a gene for which at least a short amino acid sequence of the encoded protein is known. The court held that knowledge of protein/amino acid sequence does not render the nucleic acid sequence *prima facie* obvious even in conjunction with a reference indicating a general method of cloning. In support of its holding the court pointed to the degeneracy of the genetic code and that, given the infinite possibilities suggested by the prior art, and the failure of the prior art to suggest which of those possibilities is the claimed sequence(s), the claimed sequence(s) would not have been obvious.

The Examiner has provided no evidence that the antibodies described in the cited references comprise the nucleotides set forth in SEQ ID NOs 2 and/or 4. In fact, the Examiner states that the references do not specifically teach that the prior art antibodies are encoded by nucleotides which comprise SEQ ID NOs 2 and/or 4, or that hybridize under stringent or moderately stringent conditions to complements of SEQ ID NOS 2 and/or 4. In fact, unlike the references cited in the obviousness rejection in *In re Bell*, none of the references cited in the rejection of the instant claims provide the amino acid sequences encoded by the claimed nucleic acid sequences. The Examiner states that it appears that the prior art monoclonal antibodies are the same as the instant monoclonal antibodies. However, the Examiner fails to support this assertion, especially in view of *In re Bell*. In the instant application, Applicants are not claiming all of the nucleic acid molecules that might potentially code for an antibody that binds TNF-α. Rather, Applicants claim only the nucleic acid molecules which hybridize to the complements of sequences designated by SEQ ID NOs 2, 3, 4 and 5, under conditions of high stringency, and their complements. Claims 3, 15 and 20, directed to nucleic acid molecules which hybridize under conditions of moderate stringency, have been cancelled.

Because the Examiner has not met the burden of establishing that the prior art, either separately or in combination, would have suggested the claimed sequences, the combination of the prior art references does not render the claimed invention obvious. Reconsideration and withdrawal of the rejection are respectfully requested.

Rejection of Claims 10-23 under the doctrine of obviousness-type double patenting

Claims 10-23 are rejected under the judicially-created doctrine of obviousness-type double patenting as being unpatentable over Claims 1-4 of U.S. Patent No. 6,277,969.

Applicants respectfully disagree. Claims 1-9 are not subject to this rejection. Therefore, Claims 10-12, which claim the expression vectors comprising the nucleic acid molecules recited in Claims 4-6, should not be subject to this rejection either. Furthermore, Claims 13-15 are subject to the rejection, although they only differ from Claims 1-3 in that they contain specific wash conditions. No wash conditions are recited in Claims 1-4 of U.S. Patent No. 6,277,969. Moreover, Claims 18-23 differ from Claims 1-6 solely in that they state that the recited polypeptide binds and inhibits hTNF-α whereas Claims 1-6 recite that the polypeptide only binds to hTNF-α. Neither binding nor inhibition is recited in Claims 1-4 of U.S. Patent No. 6,277,969.

Therefore, Applicants respectfully submit that Claims 10-23, like Claims 1-9, in the present invention have a different scope and are patentably distinct with respect to the Claims 1-4 of U.S. Patent No. 6,277,969. Reconsideration and withdrawal of the rejection are respectfully requested.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned at (978) 341-0036.

Respectfully submitted,

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MARKED UP VERSION OF AMENDMENTS

Specification Amendments Under 37 C.F.R. § 1.121(b)(1)(iii)

Replace the paragraph at page 1, lines 4 through 18 with the below paragraph marked up by way of bracketing and underlining to show the changes relative to the previous version of the paragraph.

This application is a continuation [divisional] of U.S. Application Serial No. 09/133,119, filed August 12, 1998, now U.S. Patent No: 6,277,969, which is a divisional of U.S. Application Serial No. 08/570,674, filed December 11, 1995, which is a continuation-in-part of U.S. Application Serial No. 08/324,799, filed October 18, 1994, now U.S. Patent No. 5,698,195, issued December 16, 1997, which is a continuation-in-part of U.S. Application Serial Nos. 08/192,102, now U.S. Patent No. 5,656,272, issued August 12, 1997, 08/192,861, now U.S. Patent No. 5,919,452, issued July 6, 1999, and 08/192,093, all filed on February 4, 1994 which are continuations-in-part of U.S. Application Serial No. 08/010,406, filed January 29, 1993, now abandoned, and U.S. Application Serial No. 08/013,413, filed February 2, 1993, now abandoned, which is a continuation-in-part of U.S. Application Serial No. 07/943,852, filed September 11, 1992, now abandoned, which is a continuation-in-part of U.S. Application Serial No. 07/853,606, filed March 18, 1992, now abandoned, which is a continuation-in-part of U.S. Application Serial No. 07/670,827, filed March 18, 1991, now abandoned. Each of the above applications are entirely incorporated herein by reference.